

REMARKS

Reconsideration is requested.

The Examiner interview of December 1, 2005 is acknowledged, with appreciation. The Examiner interview is accurate in its brief statement of the issues discussed.

Claims 25, 27, 29, 31, 35, 37, 39, 41, 45, 47, 49, 53, 55 and 57 will be pending upon the entry of the present Amendment. Claims 1-24, 26, 28, 30, 32-34, 36, 38, 40, 42-44, 46, 48, 50-52, 54 and-56 have been canceled, without prejudice. The claims have been amended to advance prosecution, without prejudice.

The Section 112, first paragraph, rejection of claims 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54 and 56 stated in the 3rd paragraph of the Office Action dated September 23, 2005, will be moot upon entry of the present Amendment. Entry of the present Amendment is requested therefore to, at a minimum, reduce the issues for appeal.

The Section 112, first paragraph "enablement", rejection of claims 24-57 stated on pages 2-4 of the Office Action dated September 23, 2005, is traversed.

Reconsideration and withdrawal of the rejection are requested in view of the following further comments.

A similar rejection, although within the context of Section 112, first and second paragraph rejections, has been made by the present Examiner in the applicants copending application Serial No. 08/362,455. The applicants submitted the following analysis in response to the rejection in the copending application, which is repeated here for completeness.

The applicants submit that one of ordinary skill in the art would be able to make and use the claimed invention without undue experimentation.

Upon entry of the present Amendment, the claims will not require hybridization, as suggested by the Examiner as a basis for the rejection. The present claims relate, in part, to HCV polynucleic acids consisting of at least 8 contiguous nucleotides of specifically recited sequences. The claim structure and recitation of at least 8 contiguous nucleotides is, in many respects, the same as the claims of U.S. Patent No. 6,762,024, which the present Examiner found enabled by the contents of the present specification.

As discussed with the Examiners during the interview, the claims further require the presence of at least one genotype-specific nucleotide. The specification, including the Figures, describe genotype-specific nucleotides required by the claims.

The identification of the genotype-specific nucleotides of the claims will be demonstrated further below by analyzing the polynucleic acid sequences of the disclosure. The Core/E1 region was chosen in the following analysis as the more difficult example to perform a detailed analysis of how to determine genotype-specific nucleotides in the nucleotide sequences as claimed. A similar analysis could be done for the Core region of HCV subtype 3c, as in the present application. However, the applicants believe that the analysis performed in the co-pending application and represented below should be sufficient to convince the Examiner in the present application that the claims are supported by an enabling disclosure which adequately describes the claimed invention.

On page 3 of the Office Action September 23, 2005, the Examiner refers to references of Kennell (1971) and Wallace (1987) as a basis for asserting that the specification allegedly fails to enable the claims. A similar rejection was advanced by the present Examiner in the related application which issued as U.S. Patent No. 6,762,024.

As noted to the Examiner prior to issuance of the related U.S. Patent No. 6,762,024, the fragment of Wallace et al. quoted by the Examiner does not exclude the possibility that probes shorter than 14 bases can be found suitable for specific hybridization, see, the wording "tendency" and "probably" in said fragment. Wallace et al. further specify that the specificity of a probe should first be determined (lines 7-8 on page 434).

In support, the applicants submit the attached two examples of successful use of probes or primers shorter than 14 nucleotides. Specifically, Majzoub et al. (1983, PNAS 258, 14061-14064; of record) successfully utilized 8-mer primers, and Chan et al. (1979, PNAS 76, 5036-504; of record) successfully utilized 10-mer probes.

Moreover, as discussed with the Examiners during the interview, genotype specific differences e.g. between HCV subtype 1a and 1b, can be detected based on probes with a difference of only 1 nucleotide. The specification, including the Figures, describe genotype-specific nucleotides required by the claims.

As also explained by the inventor during the interview with the Examiners, the definition of genotypes and subtypes of the claims are well understood from the present specification (more specifically, see pages 8 to 10) and generally advanced level of skill in the art (more specifically, see summary of the art in Table 3 on page 11 of the specification).

The requirement for a genotype-specific nucleotide, not only distinguishes the claims over the art but may also provide distinctions in identification, treatment and disease outcome, for example, as discussed with the Examiners during the interview. For Example, determination of HCV genotype is currently mandated by the FDA prior to determination of the duration of interferon/ribavirin treatment.

The following examples of genotype/subtype specific nucleotides in Core/E1 region are further provided from the specification, by way of example.

The specification describes genotype-specific amino acids in the new HCV amino acid sequences of the invention, see penultimate paragraph on page 4. The specification further teaches that, at the nucleotide level, additional genotype-specific residues are discerned due to the fact that not all differences in nucleotide sequence are translated into differences in amino acid sequence, as will be expected by one of ordinary skill in the art. See penultimate paragraph on page 3.

The specification moreover discloses amino acid sequence regions (9 to 14 consecutive amino acids in length) that in fact are specific to an HCV genotype or subtype, see pages 35-38. The ordinarily skilled person will understand from this that genotype-specific nucleotides can be determined in the same manner as genotype-specific amino acids.

At the suggestion of the Examiners during the interview, the applicants also demonstrate in the following analysis that the written description of the present application provides ample basis for the claimed invention which recite at least one genotype-specific nucleotide.

For this analysis, the Examiner is referred to the following reproductions of the Figures of the application. Specifically, the following are a duplicate of pages 26/111 to 49/111 of Figure 4 of the present application with additional sequence information relating to sequences PC-3-4, PC-3-8, PC-2-1, PC-2-6 and PC C/E1 from Figure 9 of the application having been added in hand-written text for the convenience of the Examiner. The following reproductions provide an alignment of the nucleotide sequences of different HCV subtypes (subtype 2d, subtype 3a, type 4, subtype 5a isolates) with known sequences from the corresponding region of type 1 and type 2 and type 3. This region, i.e., the Core/E1 region is, in comparison with other coding sequence regions, relatively well conserved and was therefore elected as the more difficult example to perform an exemplary analysis of the description of genotype-specific nucleotides in the nucleotide sequences of the claims and specification.

Nucleotides at a certain position from a sequence with a given SEQ ID NO (i.e. representing a specific subtype) differing from other nucleotides of known or new subtypes at the same position in the alignment are considered genotype-specific nucleotides. Vertical lines are meant to promote reading of the aligned sequences. The applicants believe that this analysis is described in the specification and can be performed by one of ordinary skill in the art to, for example, delineate a region of at least 8 contiguous nucleotides containing at least one genotype-specific nucleotide, around the genotype-specific nucleotides indicated in the following, and more generally, in all other claimed sequences.

Figure 4			379	390	400	410	420	428	WFO 8/25/01
SEQ ID NO			379	390	400	410	420	428	
HCV-1	1a		ACGTGCGGCTTCGCGGACCTCATGGGGTACATACCGCTCGTCGGGCGCC						
HCV-EC1	1a								
HCVHCT18	1a								
HCVHCT23	1a								
HCVHCT27	1a								
HCVTH	1a								
HCV-J	1b								
HC-J6	2a								
HC-J8	2b								
NE92	2d	143							
HD10	3a	13, 15, 17							
BR33	3a	23, 25, 27							
BR36	3a	19, 21							
NZL15	3a								
HCV-TR	3b								
GB809_4	4a	189							
GB116	4c	183							
GB215	4c	185							
GB358	4c	119, 187							
GB809_2	4e	122, 169							
CAM600	4e	167							
CAMG22	4f	171							
CAMG27	4f	173							
GB549	4g	120, 175							
GB438	4h	177							
CAR4/1205	4i	179							
SUBSTITUTE SHEET (RULE 26)									
Figure 4 - Continued 1									
CAR4/901	4f	181							
BE95	5a	153							
BE100	5b	155							
PC-3.4	5a	49							
PC-3.8	5a	51							
PC-4-1	5a	45							
PC-4-6	5a	47							
PC-4E1	5a	53							
SUBSTITUTE SHEET (RULE 26)									

Figure 4 : Continued 2		460	470	480	490	500	510	520	530	540	550	560	570	580	590	600	610	620	630	640	650	660	670	680	690	700	710	720	730	740	750	760	770	780	790	800	810	820	830	840	850	860	870	880	890	900	910	920	930	940	950	960	970	980	990	1000	1010	1020	1030	1040	1050	1060	1070	1080	1090	1100	1110	1120	1130	1140	1150	1160	1170	1180	1190	1200	1210	1220	1230	1240	1250	1260	1270	1280	1290	1300	1310	1320	1330	1340	1350	1360	1370	1380	1390	1400	1410	1420	1430	1440	1450	1460	1470	1480	1490	1500	1510	1520	1530	1540	1550	1560	1570	1580	1590	1600	1610	1620	1630	1640	1650	1660	1670	1680	1690	1700	1710	1720	1730	1740	1750	1760	1770	1780	1790	1800	1810	1820	1830	1840	1850	1860	1870	1880	1890	1900	1910	1920	1930	1940	1950	1960	1970	1980	1990	2000	2010	2020	2030	2040	2050	2060	2070	2080	2090	2100	2110	2120	2130	2140	2150	2160	2170	2180	2190	2200	2210	2220	2230	2240	2250	2260	2270	2280	2290	2300	2310	2320	2330	2340	2350	2360	2370	2380	2390	2400	2410	2420	2430	2440	2450	2460	2470	2480	2490	2500	2510	2520	2530	2540	2550	2560	2570	2580	2590	2600	2610	2620	2630	2640	2650	2660	2670	2680	2690	2700	2710	2720	2730	2740	2750	2760	2770	2780	2790	2800	2810	2820	2830	2840	2850	2860	2870	2880	2890	2900	2910	2920	2930	2940	2950	2960	2970	2980	2990	3000	3010	3020	3030	3040	3050	3060	3070	3080	3090	3100	3110	3120	3130	3140	3150	3160	3170	3180	3190	3200	3210	3220	3230	3240	3250	3260	3270	3280	3290	3300	3310	3320	3330	3340	3350	3360	3370	3380	3390	3400	3410	3420	3430	3440	3450	3460	3470	3480	3490	3500	3510	3520	3530	3540	3550	3560	3570	3580	3590	3600	3610	3620	3630	3640	3650	3660	3670	3680	3690	3700	3710	3720	3730	3740	3750	3760	3770	3780	3790	3800	3810	3820	3830	3840	3850	3860	3870	3880	3890	3900	3910	3920	3930	3940	3950	3960	3970	3980	3990	4000	4010	4020	4030	4040	4050	4060	4070	4080	4090	4100	4110	4120	4130	4140	4150	4160	4170	4180	4190	4200	4210	4220	4230	4240	4250	4260	4270	4280	4290	4300	4310	4320	4330	4340	4350	4360	4370	4380	4390	4400	4410	4420	4430	4440	4450	4460	4470	4480	4490	4500	4510	4520	4530	4540	4550	4560	4570	4580	4590	4600	4610	4620	4630	4640	4650	4660	4670	4680	4690	4700	4710	4720	4730	4740	4750	4760	4770	4780	4790	4800	4810	4820	4830	4840	4850	4860	4870	4880	4890	4900	4910	4920	4930	4940	4950	4960	4970	4980	4990	5000	5010	5020	5030	5040	5050	5060	5070	5080	5090	5100	5110	5120	5130	5140	5150	5160	5170	5180	5190	5200	5210	5220	5230	5240	5250	5260	5270	5280	5290	5300	5310	5320	5330	5340	5350	5360	5370	5380	5390	5400	5410	5420	5430	5440	5450	5460	5470	5480	5490	5500	5510	5520	5530	5540	5550	5560	5570	5580	5590	5600	5610	5620	5630	5640	5650	5660	5670	5680	5690	5700	5710	5720	5730	5740	5750	5760	5770	5780	5790	5800	5810	5820	5830	5840	5850	5860	5870	5880	5890	5900	5910	5920	5930	5940	5950	5960	5970	5980	5990	6000	6010	6020	6030	6040	6050	6060	6070	6080	6090	6100	6110	6120	6130	6140	6150	6160	6170	6180	6190	6200	6210	6220	6230	6240	6250	6260	6270	6280	6290	6300	6310	6320	6330	6340	6350	6360	6370	6380	6390	6400	6410	6420	6430	6440	6450	6460	6470	6480	6490	6500	6510	6520	6530	6540	6550	6560	6570	6580	6590	6600	6610	6620	6630	6640	6650	6660	6670	6680	6690	6700	6710	6720	6730	6740	6750	6760	6770	6780	6790	6800	6810	6820	6830	6840	6850	6860	6870	6880	6890	6900	6910	6920	6930	6940	6950	6960	6970	6980	6990	7000	7010	7020	7030	7040	7050	7060	7070	7080	7090	7100	7110	7120	7130	7140	7150	7160	7170	7180	7190	7200	7210	7220	7230	7240	7250	7260	7270	7280	7290	7300	7310	7320	7330	7340	7350	7360	7370	7380	7390	7400	7410	7420	7430	7440	7450	7460	7470	7480	7490	7500	7510	7520	7530	7540	7550	7560	7570	7580	7590	7600	7610	7620	7630	7640	7650	7660	7670	7680	7690	7700	7710	7720	7730	7740	7750	7760	7770	7780	7790	7800	7810	7820	7830	7840	7850	7860	7870	7880	7890	7900	7910	7920	7930	7940	7950	7960	7970	7980	7990	8000	8010	8020	8030	8040	8050	8060	8070	8080	8090	8100	8110	8120	8130	8140	8150	8160	8170	8180	8190	8200	8210	8220	8230	8240	8250	8260	8270	8280	8290	8300	8310	8320	8330	8340	8350	8360	8370	8380	8390	8400	8410	8420	8430	8440	8450	8460	8470	8480	8490	8500	8510	8520	8530	8540	8550	8560	8570	8580	8590	8600	8610	8620	8630	8640	8650	8660	8670	8680	8690	8700	8710	8720	8730	8740	8750	8760	8770	8780	8790	8800	8810	8820	8830	8840	8850	8860	8870	8880	8890	8900	8910	8920	8930	8940	8950	8960	8970	8980	8990	9000	9010	9020	9030	9040	9050	9060	9070	9080	9090	9100	9110	9120	9130	9140	9150	9160	9170	9180	9190	9200	9210	9220	9230	9240	9250	9260	9270	9280	9290	9300	9310	9320	9330	9340	9350	9360	9370	9380	9390	9400	9410	9420	9430	9440	9450	9460	9470	9480	9490	9500	9510	9520	9530	9540	9550	9560	9570	9580	9590	9600	9610	9620	9630	9640	9650	9660	9670	9680	9690	9700	9710	9720	9730	9740	9750	9760	9770	9780	9790	9800	9810	9820	9830	9840	9850	9860	9870	9880	9890	9900	9910	9920	9930	9940	9950	9960	9970	9980	9990	10000	10010	10020	10030	10040	10050	10060	10070	10080	10090	10100	10110	10120	10130	10140	10150	10160	10170	10180	10190	10200	10210	10220	10230	10240	10250	10260	10270	10280	10290	10300	10310	10320	10330	10340	10350	10360	10370	10380	10390	10400	10410	10420	10430	10440	10450	10460	10470	10480	10490	10500	10510	10520	10530	10540	10550	10560	10570	10580	10590	10600	10610	10620	10630	10640	10650	10660	10670	10680	10690	10700	10710	10720	10730	10740	10750	10760	10770	10780	10790	10800	10810	10820	10830	10840	10850	10860	10870	10880	10890	10900	10910	10920	10930	10940	10950	10960	10970	10980	10990	11000	11010	11020	11030	11040	11050	11060	11070	11080	11090	11100	11110	11120	11130	11140	11150	11160	11170	11180	11190	11200	11210	11220	11230	11240	11250	11260	11270	11280	11290	11300	11310	11320	11330	11340	11350	11360	11370	11380	11390	11400	11410	11420	11430	11440	11450	11460	11470	11480	11490	11500	11510	11520	11530	11540	11550	11560	11570	11580	11590	11600	11610	11620	11630	11640	11650	11660	11670	11680	11690	11700	11710	11720	11730	11740	11750	11760	11770	11780	11790	11800	11810	11820	11830	11840	11850	11860	11870	11880	11890	11900	11910	11920	11930	11940	11950	11960	11970	11980	11990	12000	12010	12020	12030	12040	12050	12060	12070	12080	12090	12100	12110	12120	12130	12140	12150	12160	12170	12180	12190	12200	12210	12220	12230	12240	12250	12260	12270	12280	12290	12300	12310	12320	12330	12340	12350	12360	12370	12380	12390	12400	12410	12420	12430	12440	12450	12460	12470	12480	12490	12500	12510	12520	12530	12540	12550	12560	12570	12580	12590	12600	12610	12620	12630	12640	12650	12660	12670	12680	12690	12700	12710	12720	12730	12740	12750	12760	12770	12780	12790	12800	12810	12820	12830	12840	12850	12860	12870	12880	12890	12900	12910	12920	12930	12940	12950	12960	12970	12980	12990	13000	13010	13020	13030	13040	13050	13060	13070	13080	13090	13100	13110	13120	13130	13140	13150	13160	13170	13180	13190	13200	13210	13220	13230	13240	13250	13260	13270	13280	13290	13300	13310	13320	13330	13340	13350	13360	13370	13380	13390	13400	13410	13420	13430	13440	13450	13460	13470	13480	13490	13500	13510	13520	13530	13540	13550	13560	13570	13580	13590	13600	13610	13620	13630	13640	13650	13660	13670	13680	13690	13700	1371
------------------------	--	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	-------	------

Figure 4 : Continued 4

		479	480	500	510	520	528
HCV-1	1a	ACGGCGTGAACATATGCAACAGGGAACCTTCCTGGTTGCTCTTCTCTATC					
HCVBC1	1a	-----					
HCVHCT18	1a	-----					
HCVHCT23	1a	-----C--T-----					
HCVHCT27	1a	-----					
HCVTH	1a	-----C-----					
HCV-J	1b	-----T--G--C-----					
HC-J6	2a	---G--T--T--T-----T--A--C-----C--T-----					
HC-J6	2b	---GA--A--T--C-----TT--A--C-----T-----					
NE92	2d	---GA--A-----T--G--C-----C--T-----					
HD10	3a	---GA--A--T--TC-----TT--G--C-----C--T-----					
BR13	3a	---GA--A-----TC-----TT--G--C-----T-----					
BR16	3a	---GA--A--T--TC-----TT--G--C-----C--T-----T					
NZL15	3a	---GA--A--T--TC-----T--G--C-----C--T-----					
HCV-TR	3b	---A-----T-----C--T-----T-----					
GB809_4	4a	---GA--T-----G-----T-----C-----					
GB116	4c	---TA--T--T-----T--C--C-----T-----					
GB215	4c	---A--C--T-----T--C--C-----					
GB158	4c	---GA--C--T-----G-----T-----C-----					
GB809_2	4e	---GA--C-----C-----T--C--C-----C--T-----					
CAM600	4e	---GA--C--T-----C-----C-----C--T-----					
CAMG22	4f	---GA--T-----C-----C--T-----					
CAMG27	4f	---GA--A-----T-----T-----					
GB549	4g	---GA--T-----T-----C-----C--T-----					
GB438	4h	---GA--C--T--C-----C--C-----C--T-----					

SUBSTITUTE SHEET (RULE 26)

30/11/11

WO 2015/01523

FIGURE 4 (CONTINUED)

Figure 4 - Continued 5

CAR4/1205	41	---GA--C--T-----T-----			
CAR4/901	47	---GA--T-----C-----T-----			
BE95	5a	---G--A-----C-----TT--A--C-----			
BE100	5a	---G-----T-----T--G-----			
PL-3-1	5a	G		TT A C	
PL-3-2	5a	G	C	TT A C	
PL-4-1	5a	G		TT A C	
PL-4-6	5a	G		TT A C	
PL-4-6	5a	G	S	TT A C	

SUBSTITUTE SHEET (RULE 26)

31/11/11

WO 2015/01523

FIGURE 4 (CONTINUED)

Figure 4 : Continued 6

		529	530	531	532	533	534	535	536	537	538
HCV-1	1a	TTCTTCTGCTCTCTCTGCTTGACCTGTCCTCCGCTTCGGCTACCA									
HCV-1	1a	---	T	---	---	---	---	---	---	---	---
HCVHCT18	1a	---	---	---	C	---	---	---	A	C	---
HCVHCT23	1a	---	A	---	C	---	---	---	A	---	---
HCVHCT27	1a	---	T	---	C	---	---	---	A	---	---
HCVTH	1a	---	---	---	TC	---	---	---	A	---	---
HCV-J	1b	---	CT-A	TT	G	---	T	---	CA-C	A	---
		---	---	---	---	---	---	---	---	---	---
HC-J6	2a	---	T-G	---	G-C	---	A-C	CACC	G-TC	C	TGC-G
HC-J8	2b	---	T-G	T	T-G	A	G-C	A	A-TG	T	ACTGC
S83	2c	---	---	---	---	---	---	---	---	---	STGG
NE92	2d	---	T-AT	---	A	---	TA-C	---	G-TC	C-G	TG
		---	---	---	---	---	---	---	---	---	---
HD10	3a	---	T	T	T	---	A	CCCT	A	AG	TAGTCTAG
BR33	3a	---	T	T	T	---	A	CCCT	A	AG	T-GTCTAG
BR36	3a	---	T	T	T	---	A	CCCT	A	AG	TAGTCTAG
NZL15	3a	---	T	T	T	---	A	CCCT	A	AG	CAGTCTAG
HCV-TR	3b	---	C-C	T-CT	C	---	---	---	---	---	T-G-TAG

SUBSTITUTE SHEET (RULE 26)

32/111

WO 94/25601

FIG. 4 (continued)

Figure 4 - Continued 7

		529	530	531	532	533	534	535	536	537	538
GB809_4	4a	---	C	---	A	T	T	G	C	C	A-G
Z4	4a	---	---	---	---	---	---	---	---	---	TG-G
Z1	4b	---	---	---	---	---	---	---	---	---	G-G
GB116	4c	---	C	CT	A	T	T	G	C	---	GT-A
GB215	4c	---	A	CT	A	T	T	G	C	---	AT
GB358	4c	---	CT	A	T	T	T	G	C	---	GT-A
Z6	4c	---	---	---	---	---	---	---	---	---	GT-A
Z7	4c	---	---	---	---	---	---	---	---	---	GT-A
DK13	4d	---	---	---	---	---	---	---	---	---	---
GB809_2	4e	---	CT	A	T	T	G	C	C	---	G-GTTA
CAM600	4e	---	CT	G	C	C	C	C	---	---	GTTA
G22	4f	---	---	A	T	T	G	C	---	---	TGTC
G27	4f	---	---	A	T	T	G	C	---	---	TGTC
GB549	4g	---	---	A	A	T	T	G	C	---	GC-G
GB438	4h	---	CT	A	T	T	G	C	A	---	T-TC-G
CAR4/1205	4i	---	C	T	A	T	T	G	C	---	A-AT
CAR4/901	4j	---	N	---	A	T	T	G	C	---	TC-G
		---	---	---	---	---	---	---	---	---	---
BE95	5a	---	T	T	T	T	G	TC	C	T	G-C
BE100	5a	---	T	T	T	T	G	TC	C	T	G-C
SA4	5a	---	---	---	---	---	---	---	---	---	---
PC-3-4	5a	---	T	T	T	T	G	TC	C	T	G-C
PC-3-8	5a	---	T	T	T	T	G	TC	C	T	G-C
PC-4-1	5a	---	T	T	T	T	G	TC	C	T	G-C
PC-4-6	5a	---	T	T	T	T	G	TC	C	T	G-C
PC-4/E1	5a	---	T	T	T	T	G	TC	C	T	G-C

SUBSTITUTE SHEET (RULE 26)

33/111

WO 94/25601

FIG. 4 (continued)

Figure 4 - Continued 8			579	600	610	620	628
HCV-1	1a		AGTGGCGCAACTCCACGGGGCTTTACCAAGTCACCAATGATTGCCCTAACT				
HCV-1	1a		-----T-----T-----				
HCVHCT18	1a		-----T-----T-----				C
HCVHCT23	1a		-----T-----T-----				
HCVHCT27	1a		-----A-----T-----CA-----T-----				T
HCVTH	1a		-----T-----T-----C-----C-----				C
HCV-J	1b		G-----GTGT-C-----A-A-----T-----G-C-C-----T-C-----				
HC-J6	2a		-----AAG-----AT-----GTACCGG-----ATG-----G-----C-C-----A-C-----TG				
HC-J8	2b		-----CA-G-----ATT-GTTCTAGC-----T-----C-----T-----T-A-----A				
S83	2c		G-----CAAGG-----A-----GGC-ACTCC-----ATGCCG-----C-----T-C-----				
NE92	2d		G-----CAAG-----A-----GCA-CTC-----ATG-----A-----C-----C-----G-----A				
HD10	3a		GTG-----G-----A-CT-T-C-C-----TGT-C-T-----C-C-----TT-C-----TA				
BR23	3a		GTG-----G-----TA-GT-T-C-C-----TGT-C-T-----C-C-----TT-C-----TA				
BR36	3a		GTG-----G-----TA-GT-T-C-C-----TGT-C-T-----C-C-----TT-C-----TA				
NZL15	3a		GTG-----G-----TA-GT-T-C-C-----GT-C-T-----C-C-----TT-C-----TA				
HCV-TR	3b		GTACACG-----A-GT-T-C-A-----TGTGC-T-----C-C-----T-----TG				
SUBSTITUTE SHEET (RULE 29)							
Figure 4 - Continued 9			579				628
GB809_4	4a		CTAC-----G-----TG-TT-----CA-C-----T-----A-----C-----T-----G-----T-----				
Z4	4a		CTAC-----G-----TG-TT-----CA-C-----T-----A-----C-----T-----G-----T-----				
Z1	4b		CTAC-----G-----TG-TT-----CG-C-----T-----T-----C-----T-----G-----T-----				
GB116	4c		CTAT-----G-----T-----CG-C-----T-----TA-----C-----G-----T-----				
GB215	4c		CTAT-----TG-----T-----CG-C-----T-----A-----C-----G-----T-----				
GB353	4c		CTAT-----TG-----T-----CG-C-----T-----A-----C-----G-----T-----				
Z6	4c		CTAT-----TG-----T-----CG-C-----T-----A-----C-----G-----T-----				
Z7	4c		CTAT-----TG-----T-----CG-C-----T-----A-----C-----G-----T-----				
DK13	4d		CTAT-----AG-----T-----TG-----C-----T-----C-----G-----T-----				
GB809_2	4e		CTAT-----TG-TT-----CG-----T-----A-----C-----C-----G-----TG				
CAM600	4e		CTAT-----TG-TT-----CA-----T-----A-----C-----C-----G-----TG				
G22	4f		TTAT-----A-----A-----T-----CA-C-----T-----A-----T-----C-----				
G27	4f		TTAT-----A-----A-----T-----CA-C-----T-----A-----T-----C-----				
GB549	4g		CTAC-----G-----AT-----T-----CA-----T-----C-----G-----				
GB438	4h		CTAC-----G-----TG-AT-----CA-C-----T-----C-----C-----G-----				
CAR4/1205	4i		CTAT-----TG-TT-----ACGG-----TT-TA-----C-----G-----				
CAR4/901	4j		CTAC-----G-----TGT-T-----CA-C-----T-----G-----T-----				
BE95	5a		CTAC-----A-----TG-----T-----T-----A-----T-----T-----T-----A-----				
BE100	5a		CTAC-----A-----TG-----T-----T-----A-----C-----T-----T-----A-----				
SA4	5a		CTAC-----A-----G-----T-----T-----G-----T-----T-----A-----				
PL-3.4	5a		CTAC A TG T T A T T				
PL-3.8	5a		CTAC A TG T T A T T				
PL-4.1	5a		CTAC A TG T T A T T				
PL-4.6	5a		CTAC A TG T T A T T				
PL-4/E1	5a		CTAC A TG T T A T T				
SUBSTITUTE SHEET (RULE 29)							

Figure 4 - Continued 10

		629	640	650	660	670	678
HCV-1	1a	CGAGTATTCGTGTCGAGGCGGCGGATGCCATCCTGCACACTCCGGGGTGC					
HCV-EC1	1a	-----	-----	-----	-----	-----	-----
HCVHCT18	1a	-----	A-----	A-----	C-----	-----	-----
HCVHCT23	1a	-----	-----	-----	-----	G-----	-----
HCVHCT27	1a	-----	-----	A-----	CA-----	A-----	-----
HCVTH	1a	-----	-----	-----	T-----	G-----	-----
HCV-J	1b	A-----	T-----	A-----	G-CATG-----	A-----	C-C-----
HC-J6	2a	AT--C--ACC-GGC-ACTCCAG-C--TG--C--GTC-C-----					
HC-J8	2b	AC--C--CACC-GGC-CTCA-T--C--AG-T--C--TCT--T--A--					
S83	2c	T--C--T--GGC-CTT-AA-GA--AG-G--T--T--T--A--					
NE92	2d	GT--C--C--C-GGC-CTCAGG--TG-T--T--GTC-C-----					
HD10	3a	GC-----T-----C-AT-C-TT-T-----A-C-C-T					
BR33	3a	GT-----T-----C-AT-C-TT-T-----G-G-C-C-T					
BR36	3a	GC-----T-----C-AT-C-TT-T-----A-C-C-C					
NZL15	3a	GC-----T-----C-AT--T--T-----A-C-C-C-T					
HCV-TR	3b	G--C-----C-AA--TG--T--TTA--C-A--					

Figure 4 - Continued 11

		629					678
GB809_4	4a	-C--C--A--C--T--AA-T-A-C-CCAT--AT--TTG-----					
Z4	4a	-C--C--A--C--T--A--T-A-C-CA-----A--TTG-----					
Z1	4b	-C--C--A--T-----A--ASC-CCA-----A--TTG-A-----T					
GB116	4c	-C--C--A--T-----T-A-T-CCA-----A--CTC-T-----					
GB215	4c	-C--C--A--T-----C-A-C-CCA-----A--CT--A-----					
GB359	4c	-C--C--A--T-----A-C-ASC-CCA-----A--CTC-A-----T					
Z6	4c	-C--C--A--T-----C-AAC-CCAG--T-A--CTC-A-----					
Z7	4c	-C--C--AA--T-----C-AAC-CCA-----A--CTC-A-----					
UK13	4d	-C--C--A--C--T--AA-C-TT-CCA-----T-A--CTC-A-----					
GB809_2	4e	-C--C--A--T-----A-C-A-A-CA-----T-A--CTC-A-----					
CAM500	4e	-A--C--A--T-----A-C-AAA-CA-----T-A--CTC-A-----					
G22	4f	-T--C--A--C--T--A--C-C-CA-----T--CT--A--A-----					
G27	4f	-T--C--A--C--T--A--ASC-CA-----T--TCT--A--A-----					
GB549	4g	-T--C--A--T-----T-A-T-A-C-CAT--A--TCTA-A-----T					
GB438	4h	-C--C--A--T-----T-A-C-A-C-CA-----A--CTA-C-----T					
CAR4/1205	4i	-T--C--A--T-----T-A-C-AGA-CCA-----T--CT-----T					
CAR4/901	4j	-C--C--A--T-----T-A-C-ATC-CCA-----A--TTA-A-----					
BE95	5a	-TTCC--A--C--T-----A-ATA-CCTG-----A--G-A-T--T--					
BE100	5a	-TTCC--A--C--T-----A-AT--CTG-----A--G-A-T--C--					
SA4	5a	-TTCC--A--T-----T-ATA-CCTG-----T--TG-A-T--T--					
PC-3.3	5a	TTCC--A--C--T-----A-ATA-CCTG-----A--G-A-T--T--					
PC-3.8	5a	TTCC--A--C--T-----A-ATA-CCTG-----A--G-A-T--T--					
PC-4.1	5a	TTCC--A--C--T-----A-ATA-CCTG-----A--G-A-T--T--					
PC-4.6	5a	TTCC--A--C--T-----A-ATA-CCTG-----A--G-A-T--T--					
PC-C/E1	5a	TTCC--A--C--T-----A-ATA-CCTG-----A--G-A-T--T--					

Figure 4 - Continued 12

		679	690	700	710	720	728
HCV-1	1a	GTCCCTTCGTTTTCGAGGGCAACGCCTCGAGGTGTTGGGTGGCGATGAC					
HCV-1	1a	-----AC-----T-----					
HCVHCT18	1a	-----AC-----T-----G-----					
HCVHCT23	1a	-----C---AT---T---A-----G-----					
HCVHCT27	1a	-----C---T-----AA-----C-G-AG-					
HCVTH	1a	-----C---T-----					
HCV-J	1b	--G-C---C-G---A-T---TTT---CC-T-C---A-C-C-					
HC-J6	2a	-----G---ACAA-T---G-TA-A---TC---C---A-AC-G-CT-					
HC-J8	2b	-----A-T-ACAA---TAATGG-A---T-CAT-C---A-ACAAG-A-					
S83	2c	-----T-AG---ACC-C---T---TC-A-----C-G-TG-					
NE92	2d	-----T-ACGAGA-----ATA-CC-C---A-AC-G-TT-					
HD10	3a	--A---T---AG-C-T---TA-A-TGC---C---ACCC-AG---					
BR33	3a	--A---T---C-AG-C---TA-G-T-CA-C---ACCC-AG-A---					
BR36	3a	A-A---T---C-AG-C---TA-A-C-C---C---ACCC-AG---					
NZL15	3a	--A---T---C-AG-C---TA-A-T-C---C---ACCC-AG---					
HCV-TR	3b	--G-C---CACAACC---CAA-ATCA-C---ACAA-G-CT-					

SUBSTITUTE SHEET (RULE 26)

39/111

WO 04/25611

PCR/EP/01/111

Figure 4 - Continued 13

		679				728
GB809_4	4a	--A-C---GA-G-CC-G---TG-TC-T-C---AC-C-G-A---				
Z4	4a	--A-C-T---GATGACT---G---A-A---C-T-C---AC-C-G---				
Z1	4b	-----C-T-G---GAC-AG-TA-T-TC-C-C---C-CT---				
GB116	4c	T-A-C---GA-G-TT-G---TCAG-AC-C-C---CC-T---				
GB215	4c	T-A-C-T---GA-G-TT-G---TCAG-AC-T-----CC-CT-				
GB358	4c	T-A-C---GA-G-TT-G---TCAG-AC-C-C---CC-C---				
Z6	4c	T-G-C-T---GA-G-TT-G---TCAG-AC-C-C---CC-T---				
Z7	4c	--A-C-T---GA-G---G---CAG-AC-C-C---CC-T---				
DK13	4d	--T---GA-G-A-G---AAG-T-CA-C---T-TC-C---				
GB809_2	4e	--A-C-T---GAGACC-G---CAG---C---CC-C---				
CAM600	4e	--A-C-T---GA-GACT-G---CAG---C---CC-C---				
G22	4f	-----T-AA-AACT-G---CAG-TC---C---A-CT---				
G27	4f	-----C-T---GA-AACT-G---CAG-AC-A-C---A-A-CT---				
GB549	4g	--G---GA-AACT-G---A---C-C-C---TC-TT-A---				
GB438	4h	--G-C-T---AA-AACT-G-T-T---C-T-C---A-TC-TT-A---				
CAR4/1205	4i	A-A-C-T---GAGACC-G---TCAG---C---C---TC-C---				
CAR4/901	4j	A-A-C---GA-GACC-G---TT---C-C-C---AT-TC---				
BE95	5a	--G---T---CATGACA-T-T-TGAGT---A-C---CCAA-T---				
BE100	5a	--G---T---CA-GA-A-AT-T-TGAGT---C---CCAA-T---				
SA4	5a	--G---T---CA-GC-A-AT-T-TAGT-A---C---CCAA-C---				
PC-3.4	5a	G T CATGACA T T TGAGT A C CCAA T				
PC-3.8	5a	G T CATGACA T T TGAGT A C CCAA T				
PC-4.1	5a	G T CATGACA T T TGAGT A C CCAA T				
PC-4.6	5a	G T CATGACA T T TGAGT A C CCAA T				
PC-CHE	5a	G T CATGACA T T TGAGT A C CCAA T				

SUBSTITUTE SHEET (RULE 26)

39/111

WO 04/25611

PCR/EP/01/111

Figure 4 - Continued 14

		729	730	740	750	760	770	778
HCV-1	1a	CCCTACCGTGTCTCAACAGGGA	TGGCAAACTCCCGC	SACGCAGCTTCGAC				
HCV-EC1	1a	---C---	---C---	---A---	---A---	---A---	---A---	---
HCVHCT18	1a	---C---	---C---	---A---	---A---	---A---	---A---	---
HCVHCT23	1a	---C---	---C---	---A---	---A---	---A---	---A---	---
HCVHCT27	1a	---C---	---C---	---A---	---A---	---A---	---A---	---
HCVTH	1a	---C---	---C---	---A---	---A---	---A---	---A---	---
HCV-J	1b	T---C---	C---C---	CG---	A---CA---	GCA---	A---C---	ACAA---A---
HC-J6	2a	A---G---AT---	GTCCA---C---	GCC---GGCGC---	T---A---	CA---GGCT---	A---GA	
HC-J8	2b	A---C---AC---	TGTG---AAC---	CC---GGTGCG---	T---A---	TCGTAGC---	G---A	
SR3	2c	---C---ATC---	TA---	TG---ACCTGGGCGCT---	T---A---	T---A---GGC---	G---G	
NE92	2d	G---C---ATG---	A---TGTG---	CC---ACCTGGTGCG---	TTA---C---	A---GGC---	G---GA	
HD10	3a	A---A---	AGT---	T---T---GG---GCAA---	A---CG---	TTC---	A---A---CA	
BR33	3a	A---A---	AGT---	T---T---GGGGCAA---	A---CG---	TTC---	A---A---CA	
BR36	3a	A---A---	AGT---	T---T---GG---GCAA---	A---CG---	TTC---	A---A---CA	
NZL15	3a	A---A---	AGT---	T---T---GG---GCAA---	TA---TG---	TTC---	A---A---CA	
HCV-TR	3b	AA---G---	GTT---	ACCCTTGGCG---	G---	A---CG---	TC---	A---C---A

SUBSTITUTE SHEET (RULE 30)

40/111

WO 94/25401

FIG. 4 (Continued)

Figure 4 - Continued 15

		729	730	740	750	760	770	778
GB809_4	4a	A---	TG---	GTATCATGG---CGCT---	GCTCGA---TCC---	C---G---		
Z4	4a	G---	A---	TGT---CAC---	CCCCGGGCGCT---	GCTTGA---TC---	T---C---G---	
Z1	4b	---C---T---	---G---CCCT---	CC---	CGCA---	GTAGA---TCCA---	G---CA	
GB116	4c	T---C---C---	GG---GCCT---	C---TTGGTGCT---	GCTAGAATCC---	C---GA		
GB215	4c	T---C---C---	GG---GCCT---	CAT---GGTGCT---	A---TTGAATCC---	C---GA		
GB359	4c	T---C---C---	GG---GCCT---	CAT---GGCGCT---	GCTTGAATCC---	C---GA		
Z6	4c	T---C---C---	GGTGCT---	AT---GGTGCT---	GCTTGAATCC---	C---GA		
Z7	4c	T---C---C---	GG---GCCT---	AT---GGTGCA---	GCTTGAATCC---	C---GA		
DK13	4d	---C---C---	TS---GAAAC---	CTG---TGCT---	GCTTGA---TCT---	GA---		
GB809_2	4e	T---C---A---	GG---GCCT---	T---T---GGTGCT---	GCTCGA---CCT---	G---G---		
CAM600	4e	T---C---A---	GG---GCAT---	C---C---GGTGCT---	GCTTGA---CCT---	G---G---		
G22	4f	---C---C---	---G---GCAT---	CCTTGGGCGCT---	ACTCGA---TCCA---	G---G---		
G27	4f	---C---C---	---G---GCAT---	CATTGGGCGCT---	ACTTGA---TCCA---	G---G---		
GB549	4g	A---C---T---	TS---CTCT---	TTGGGCGG---	GCTCGAATCCA---	G---G---		
GB439	4h	A---C---T---	A---GT---CTCT---	CCT---GGGGCT---	ACTT---	TCTG---	A---G---	
CAR4/1205	4i	---C---C---	GG---CCAC---	CCTACGTGCT---	GCTTT---	TCCT---	A---GG	
CAR4/901	4j	A---T---	TS---TCCCT---	CCT---GGGGCT---	GCTT---	TC---	A---G---	
BE95	5a	---AC---	G---AG---	CC---AGCT---	GG---GCACT---	A---G---T---CT---	---GA	
BE100	5a	---C---C---	G---AG---	CC---AGCT---	GG---GCACT---	A---G---T---CT---	---GA	
SA4	5a	---C---T---	G---AG---	CC---AGCT---	GG---GCACT---	A---G---T---CT---	---GA	
PC-3-7	5a	AK---	CT---	AGCT---	GG---	GACT---	A---G---T---CT---	GA
PC-3-8	5a	AK---	CT---	AGCT---	GG---	GACT---	A---G---T---CT---	GA
PC-4-1	5a	AK---	CT---	AGCT---	GG---	GACT---	A---G---T---CT---	GA
PC-4-6	5a	AK---	CT---	AGCT---	GG---	GACT---	A---G---T---CT---	GA
PC-CE1	5a	AK---	CT---	AGCT---	GG---	GACT---	A---G---T---CT---	GA

SUBSTITUTE SHEET (RULE 30)

41/111

WO 94/25401

FIG. 4 (Continued)

Figure 4 - Continued 14

		729	730	740	750	760	770	778
HCV-1	1a	CCCTACGCTGCTCACTGGGATGGCAAACTCCCGCGACGCAGTTTCGAC						
HCV-1	1a	---C---	---C---	---C---	---C---	---A---	---A---	---
HCVHCT18	1a	---C---	---C---	---C---	---C---	---A---	---A---	---
HCVHCT23	1a	---C---	---C---	---C---	---C---	---A---	---A---	---
HCVHCT27	1a	---C---	---C---	---C---	---C---	---A---	---A---	---
HCVTH	1a	---C---	---C---	---C---	---C---	---A---	---A---	---
HCV-J	1b	T---C---	C---C---	CG---	A---CA---	GCA---	A---C---	ACAA---A---
HC-J6	2a	A---G---AT---	GTGCA---G---	GCC---GGCGC---	T---A---	CA---GGCT---	A---GA---	
HC-J8	2b	A---C---AC---	TGTG---AAC---	CC---GGTGCG---	T---A---	TCGTAGC---	G---A---	
S83	2c	---C---ATC---	---TA---	TC---ACCTGGCGCT---	T---A---	T---A---GGC---	G---G---	
NE92	2d	G---C---ATC---	---TA---	TC---ACCTGGTGCG---	TTA---C---	A---GGC---	G---GA---	
HD10	3a	A---A---	AGT---	T---C---T---GG---GCA---	A---CG---	TTC---A---	A---CA---	
BR33	3a	A---A---	AGT---	T---C---T---GGGGCAA---	A---CG---	TTC---A---	A---CA---	
BR36	3a	A---A---	AGT---	T---C---T---GG---GCA---	A---CG---	TTC---A---	A---CA---	
NZL15	3a	A---A---	AGT---	T---C---T---GG---GCA---	TA---TG---	TTC---A---	A---CA---	
HCV-TR	3b	AA---G---	GTT---	ACCCTGGCG---	GA---	A---CG---	TC---A---	C---A---

SUBSTITUTE SHEET (RULE 30)

40/111

WO 94/25401

FIG. 4 (continued)

Figure 4 - Continued 15

		729						778
GB809_4	4a	A---	---TG---	GTATCATGG---CGCT---	GCTCGA---TCCT---	C---G---		
Z4	4a	G---	---A---	TGT---CAC---	CCCAGGCGCT---	GCTTGA---TC---	T---C---G---	
Z1	4b	---C---T---	---G---	CCCT---	CC---CGCA---	GTTAGA---TCCA---	G---CA---	
GB116	4c	T---C---C---	---GG---	GCCT---	C---TTGGTGCT---	GCTAGAATCC---	C---GA---	
GB215	4c	T---C---C---	---GG---	GCCT---	CAT---GGTGCT---	A---TTGAATCC---	C---GA---	
GB358	4c	T---C---C---	---GG---	GCCT---	CAT---GGCGCT---	GCTTGAATCC---	C---GA---	
Z6	4c	T---C---C---	---GG---	GCCT---	AT---GGTGCT---	GCTTGAATCC---	C---GA---	
Z7	4c	T---C---C---	---GG---	GCCT---	AT---GGTGCA---	GCTTGAATCC---	C---GA---	
DK13	4d	---C---C---	---TG---	CAAC---	CTG---TGCT---	GCTTGA---TCCT---	GA---	
GB809_2	4e	T---C---A---	---GG---	GCCT---	C---T---GGTGCT---	GCTCGA---CCT---	G---G---	
CAM600	4e	T---C---A---	---GG---	GCCT---	C---C---GGTGCT---	GCTTGA---CCT---	G---G---	
G22	4f	---C---C---	---G---	GCCT---	CCTTGGCGCT---	ACTCGA---TCCA---	G---G---	
G27	4f	---C---C---	---G---	GCCT---	CATTGGCGCT---	ACTTGA---TCCA---	G---G---	
GB549	4g	A---C---T---	---TG---	CCCT---	TTGGCGCG---	GCTCGAATCC---	G---G---	
GB439	4h	A---C---T---	---A---	GT---CCCT---	CCT---GGGGCT---	ACTT---TCTG---	A---G---	
CAR4/1205	4i	---C---C---	---GG---	GCCT---	CCTACGTGCT---	GCTTT---TCCT---	A---GG---	
CAR4/901	4j	A---A---	---T---	TG---TCCT---	CCT---GGGGCT---	GCTT---TC---	A---G---	
BE95	5a	---AC---	---G---	AG---CC---AGCT---	GG---GCA---	T---A---G---T---CT---	---GA---	
BE100	5a	---C---C---	---G---	AG---CC---AGCT---	GG---GCA---	T---A---G---T---CT---	---GA---	
SA4	5a	---C---C---	---G---	AG---CC---AGCT---	GG---GCA---	T---A---G---T---CT---	---GA---	
PC-3-4	5a	AK---	---G---	AG---	CC---	AGCT---	GG---	GCA---
PC-3-8	5a	AK---	---G---	AG---	CC---	AGCT---	GG---	GCA---
PC-4-1	5a	AK---	---G---	AG---	CC---	AGCT---	GG---	GCA---
PC-4-6	5a	AK---	---G---	AG---	CC---	AGCT---	GG---	GCA---
PC-CE1	5a	AK---	---G---	AG---	CC---	AGCT---	GG---	GCA---

SUBSTITUTE SHEET (RULE 30)

41/111

WO 94/25401

FIG. 4 (continued)

Figure 4 - Continued 18

		829	Y40	170	16	873	878
HCV-1	1a	GTGGGGGACCTATGCGGGTCTGTCTTCTTGTGGGCCAACTGTTCACTTT					
HCVBC1	1a	-----G-----C-----T-----T-----					
HCVHCT18	1a	-----T-----G-----C-----T-----					
HCVHCT23	1a	-----T-----CA-----T-----T-----					
HCVHCT27	1a	-----T-----G-----T-----T-----					
HCVTH	1a	-----G-----CA-----T-----T-----					
HCV-J	1b	-----T-----T-----C-----A-----C-----T-----C-----TC-----G-----					
HC-J6	2a	-----C-----TGGG-----GA-----G-----CA-----C-----GA-----TTG-----					
HC-J8	2b	-----A-----TG-----G-----C-----GA-----GA-----C-----ATCG-----GGCT-----TGG-----					
S83	2c	-----G-----G-----T-----CG-----GC-----GA-----G-----G-----C-----CT-----GG-----CG-----GT-----G-----					
NE92	2d	A-A-A-----G-----T-----CG-----G-----GA-----GT-----G-----CTTCT-----G-----C-----T-A-----					
HD10	3a	-----T-----TG-----G-----T-----G-----C-----C-----C-----G-----A-----GCC-----G-----					
BR33	3a	-----T-----TG-----G-----T-----G-----C-----C-----C-----G-----A-----GCC-----G-----					
BR26	3a	-----T-----TG-----G-----T-----G-----C-----C-----C-----G-----A-----GCC-----G-----					
NZL15	3a	-----T-----TG-----G-----T-----G-----C-----C-----C-----G-----A-----GCC-----G-----					
HCV-TR	3b	-----C-----CCT-----T-----G-----G-----G-----G-----A-----GC-----					

SUBSTITUTE SHEET (RULE 26)

WFO 94/25401

45/111

PT/EP/JP/01133

Figure 4 - Continued 19

		829	Y40	170	16	873	878
GB809_4	4a	-----T-----A-----T-----T-----AGG-----CT-----C-----A-----G-----G-----GA-----					
Z4	4a	-----T-----T-----T-----T-----AGG-----C-----C-----GA-----G-----G-----GA-----A-----T-----					
Z1	4b	A-T-A-T-----G-----T-----AGGC-----C-----A-----G-----G-----GA-----					
GB116	4c	A-C-----T-----G-----T-----TGGC-----A-----T-----G-----T-----T-----GA-----TT-----T-----					
GB215	4c	A-T-----T-----G-----T-----TGGC-----A-----CT-----G-----T-----T-----GA-----TT-----T-----					
GB358	4c	A-C-A-----T-----G-----T-----TGGC-----A-----T-----G-----T-----T-----GA-----TT-----T-----					
Z6	4c	-----T-----A-----T-----G-----T-----TGG-----CA-----CT-----G-----T-----GA-----T-----					
Z7	4c	A-T-----T-----G-----T-----TGGC-----A-----T-----G-----T-----T-----GA-----TT-----T-----					
DK13	4d	A-C-A-----T-----G-----T-----GG-----G-----CT-----G-----T-----T-----GA-----TT-----T-----					
GB809_2	4e	-----C-----C-----T-----TGGCT-----A-----CT-----G-----A-----A-----					
CAM600	4e	A-C-U-----T-----G-----T-----TGGCT-----A-----CT-----G-----G-----A-----					
G22	4f	-----T-----T-----G-----T-----GGCA-----A-----C-----A-----CG-----GA-----					
G27	4f	A-T-A-T-----G-----T-----AGGCA-----A-----A-----G-----GA-----A-----					
GB549	4g	A-C-A-----T-----T-----AGG-----C-----G-----G-----GA-----					
GB438	4h	A-C-A-----T-----T-----AGG-----CT-----G-----CA-----G-----GA-----G-----GT-----					
CAR4/1205	4i	A-T-A-T-----G-----T-----GG-----G-----T-----G-----CG-----TA-----					
CAR4/901	4j	-----C-----A-----T-----AGG-----C-----A-----G-----A-----GA-----					
BE95	5a	-----A-----A-----GCG-----T-----G-----AC-----A-----CT-----G-----A-----A-----					
BE100	5a	-----T-----A-----GCG-----T-----G-----AC-----A-----T-----G-----A-----A-----					
SA4	5a	-----C-----C-----GCG-----T-----G-----A-----G-----T-----G-----A-----A-----					
PC-3.4	5a	A A GCG T G A C A CT G A A					
PC-3.2	5a	A A GCG T G A C A CT G A A					
PC-4.1	5a	A A GCG T G A C A CT G A A					
PC-4.6	5a	A A GCG T G A C A CT G A A					
PC-CE1	5a	A A GCG T G A C A CT G A A					

SUBSTITUTE SHEET (RULE 26)

WFO 94/25401

45/111

PT/EP/JP/01133

Figure 4 - Continued 20

		879	890	900	910	920	928
HCV-1	1a	CTCTCCACAGCC	CCCACTGGACG	ACGCAAGGTT	GCAATTGCTCT	ATCTATC	
HVVEC1	1a	-----	-----	-----	-----	-----	
HCVHCT18	1a	-----	-----	-----	-----	-----	
HCVHCT23	1a	-----	-----	-----	-----	-----	
HCVHCT27	1a	-----	-----	-----	-----	-----	
HCVTH	1a	-----	-----	-----	-----	-----	
HCV-J	1b	---A--TC-C-	GT-TGA-	GTA--A-	-----	-----	
HC-J6	2a	---G--ACA-A-	TTTGT--	AC--	-----	-----	
HC-J8	2b	A--A--ACAA-	AACTTC-C	AC--	-----	-----	
S83	2c	G--G--ACAA-	TAC-TTGTC-	G-AA-	-----	-----	
NE92	2d	---G--CA--AT-	TAA-TTGTC-	G-AC--	-----	-----	
HD10	3a	-AGA--TC-T-	TCGA--	GTC--GACC-	T-C--	AC--G-C-	
BR33	3a	-AGA--C-C-	TCGA--	GTC--GACC-	T-C--	GC--G-C-	
BR36	3a	-AGA--TC-T-	TCGA--	GTC--GACC-	T-C--	GC--G-C-	
NZL15	3a	-AGA--TC-A-	TCGA--	GTC--GACC-	T-C--	GC--G-C-	
HCV-TR	3b	-AGA--TC-C-	TCGA--	GTC--GACC-	T-C--	GC--G-C-	

SUBSTITUTE SHEET (RULE 26)

45/111

WO 04/25401

FIGURE 4(111)

Figure 4 - Continued 21

		879					920
GB809_4	4a	-CAC--GC-T-	-----	C--	G-A--T-	-----	A
Z4	4a	TCGG--GC-T-	-----	C--	G-AG--	T-C--	CA
Z1	4b	-CGA--GC-C-G-	-----	C--C--	G-A--	-----	C
GB116	4c	-CAG--GC-A-	-----	C--	G-AC--	T-C--	CG
GB215	4c	-CGG--AC-A-	-----	T--	G-AC--	T-C--	CG
GB358	4c	-CAG--GC-A-	-----	T--	G-AC--	T-C--	CG
Z6	4c	-CAG--GC-A-	-----	T--	G-AC--	T-C--	CG
Z7	4c	-CAG--GC-A-	-----	T--	G-AC--	T-C--	G
DK13	4d	-CAA--TC-C-	-----	C--C--	AC--	T-C--	CA
GB809_2	4e	-CAA--GC-A-	-----	C--	G-AC--	T-C--	CG
CAM600	4e	-CAA--GC-A-T-	-----	C--T--	G-AC--	T-C--	CA
G22	4f	-CGG--C-C-T-	-----	C--C--	G-AG--	T-C--	CG
G27	4f	-AGG--C-C-TG-	-----	C--C--	G-AG--	T-C--	CG
GB549	4g	-CGG--GC-C-	-----	T--	F-C--	G-AC--	C
GB438	4h	-CAA--C-C-T-T-	-----	T--	C--G-A-	-----	C
CAR4/1205	4i	-CGG--AC-C-TT-	TCGA--	C--T--	G-AC--	-----	CG
CAR4/901	4j	-CAG--GC-C-	-----	C--T--	G-AC--	-----	CG
BE95	5a	TAGG--TC-C-AG-	GGT--	GT--	GAAC--	C-T-C-	T-CA
BE100	5a	TAGG--TC-C-AG-	TGGT--	GT--	G-AC--	C-T-C-	CA
SA4	5a	TAGG--TC-C-AG-	ACT--	GT--	AC--	-----	T-CA
PL-3-4	5a	TAGG TC C AG	GGT	GT	GAAC	C T C	T CA
PL-3-8	5a	TAGG TC C AG	GGT	GT	GAAC	C T C	T CA
PL-4-1	5a	TAGG TC C AG	GGT	GT	GAAC	C T C	T CA
PL-4-6	5a	TAGG TC C AG	GGT	GT	GAAC	C T C	T CA
PL-C/E1	5a	TAGG TC C AG	GGT	GT	GAAC	C T C	T CA

SUBSTITUTE SHEET (RULE 26)

47/111

WO 04/25401

FIGURE 4(111)

Figure 4 - Continued 22

		929	940	950	957
HCV-1	1a	CCGGCCATATAACGGGTCACCGCATGGCA			
HCVHCT18	1a	-----C-----G-----			
HCVHCT23	1a	-----C-----G-----			
HCVHCT27	1a	-----A-----			
HCVTH	1a	-----C-----T-----A-----T-----			
HCV-J	1b	-----CG-----T-----A-----T-----			
HC-J6	2a	-T--TACC--C--T--A-----G			
HC-J8	2b	AA--T--C--C--C--C--T-----			
S83	2c	-G--GC--T--A-----T-----			
NE92	2d	-A-----C--C--T--A--T--G-----G			
HD10	3a	-A-----C--TT--A--A-----T-----			
BR33	3a	-A-----C--TT--A--A--T--A-----T-----			
DR36	3a	-A-----C--TT--A--A--T--A-----T-----			
NZL15	3a	-A-----C--TT--A--A--T--A-----T-----			
HCV-TR	3b	-A-----C--TT--A--A--T--T-----G			

SUBSTITUTE SHEET (RULE 29)

48/111

WO 04/25601

PC/E9/0132

Figure 4 - Continued 23

SUBSTITUTE SHEET (RULE 26)

GB809_4 4a
 Z4 4a
 Z1 4b
 GB116 4c
 GB215 4c
 GB358 4c
 Z6 4c
 Z7 4c
 DK13 4d
 GB809_2 4e
 CAM600 4e
 G22 4f
 G27 4f
 GB549 4g
 GB438 4h
 CAR4/1205 4i
 CAR4/901 4j

BE95 5a
 BE100 5a
 SA4 5a

PC-3-4 5a
 PC-3-8 5a
 PC-4-1 5a
 PC-4-6 5a
 PC-CIE1 5a

929
 929

T-----C--C--C--A--C-----G
 T-----C--C--C--A--C-----G
 T--T--C--CT--C--A--G-----C
 -G--G--CG--T--C--A--G-----
 -G--G--C--C--T--C--G--A-----
 -G--G--CG--T--C--A--G-----
 -A--G--C--C--C--A--G-----
 -G--G--CG--T--A--C--A--A-----
 -A--A--C--A--A--A--A-----T
 -A--G--T--C--T--G-----T
 -G--C--T--T--G-----
 -G--C--C--TA--A--G-----
 -A--G--C--A--A--G-----
 AT--C--C--C--TA--A--T-----
 TG--C--C--C--A--G-----C
 -A--G--C--C-----
 T-----C--C--A--C--A--A-----T

GT-----G--T--C--C-----G-----G
 GT-----CG--C--C--C--T--G-----
 GT-----C--C--C-----G-----

GT G T C C G
 GT G T C C G
 GT G T C C G
 GT G T C C G
 GT G T C C G

957

SUBSTITUTE SHEET (RULE 29)

49/111

WO 04/25601

PC/E9/0132

Withdrawal of the Section 112, first paragraph, rejection of the claims stated on pages 2-5 of the Office Action dated September 23, 2005, is requested.

The Section 112, first paragraph "written description", rejection of claims 24-57 stated on page 4 of the Office Action of September 23, 2005, is submitted to be obviated by the above amendments. Reconsideration and withdrawal of the rejection are requested as the claims do not require hybridization, as suggested by the Examiner's reference to "desired properties" as a basis of the rejection. Entry of the above amendments and withdrawal of the rejection are requested.


The present Amendment is submitted to place the application in condition for allowance without raising new issues requiring further search and/or consideration. No new matter has been added. Entry of the present Amendment and allowance of the application are requested.

The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____


B. J. Sadoff
Reg. No. 36,663

BJS:
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☒ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.